Permitting Genetically Engineered Plants That Produce Pharmaceutical Compounds

Through its Biotechnology Regulatory Services (BRS) program, the U.S. Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS) is responsible for regulating the introduction (importation, interstate movement, and field release) of genetically engineered (GE) organisms, such as plants, insects, micro-organisms, and any other organisms that are known to be or could be a plant pest. Through a strong regulatory framework, BRS works to ensure the safe and confined introduction of new GE plants, such as trees, grass, food crops, and crops grown for use in making pharmaceutical and industrial compounds.

A pharmaceutical or industrial crop is a plant that has been genetically engineered to produce a medical or industrial product, including a human or veterinary drug, biologic, industrial or research chemical, or enzyme. Examples of species that have been used to produce pharmaceutical and industrial compounds include: rice, corn, barley, tobacco, and safflower. These crops are grown to produce research chemicals, vaccines, human antibodies, and human blood proteins. Since 1991, more than 90 permits for the testing of pharmaceutical and industrial crops have been issued. Pharmaceuticals and industrials fall into a distinct category, and BRS policy makes clear that these GE plants are handled differently than those being developed for use as food or feed.

Pharmaceutical and Industrial Requirements

Developers interested in field-testing a pharmaceutical or industrial crop must obtain permission from APHIS through a permit. APHIS issues permits for pharmaceuticals and industrials on a case-by-case basis following a rigorous review process.

The developers must submit all plans for field testing for BRS' review. The purpose of the review is to ensure that the field tests are conducted in such a way that there is no harm to agriculture or the environment. A skilled staff of regulatory scientists conducts the permit reviews to evaluate the risks of the field tests or movement of the crops. The measures to confine the field trial and the potential environmental effects are also carefully evaluated. BRS employs a strong scientific basis for performing all aspects of the permitting process. BRS has experts in the fields of plant pathology, botany, entomology, ecology, virology, animal science, and molecular biology. These experts conduct extensive scientific reviews of permit applications, petitions, and potential infractions.

For field tests of pharmaceutical and industrial plants, APHIS imposes more stringent confinement measures than for field tests of conventional GE crops, such as increased isolation distances and fallow zones, and increased inspections and oversight. During the growing season, measures must be taken to achieve reproductive isolation from any sexually compatible plants to prevent cross-pollination with cultivated or wild plants that are not part of the field test. Environmental effects considered include impacts on threatened and endangered species, toxicity of the GE plant to nontarget organisms, and the likelihood of such organisms to be exposed. In cases involving new risks, such as a new species, the staff prepares an environmental assessment accompanied by a public comment period.

In 2003, BRS published two *Federal Register* notices announcing the strengthening of permit conditions for field-testing of plants engineered to produce pharmaceuticals and industrials. These regulatory changes resulted in stricter confinement measures and a greater Government role.

Regulation of Pharmaceutical and Industrial Field Trials

Permit Conditions

- Pharmaceutical and industrial crops must be separated from other sexually compatible crops by a substantial distance. For example, the isolation distance for open-pollinated corn is 1 mile, which is eight times further than is required for foundation seed production.

Other permit conditions include:

- A 50-foot fallow zone must surround the plot;
- Developers must submit for APHIS review their procedures for seed handling;
- Developers are required to have an APHIS-approved training program for their personnel;

- Developers must have equipment and storage dedicated to the pharmaceutical or industrial field trial. The same equipment and storage cannot be reused for crops beyond the field test;
- Developers may not plant food or feed crops on the land that was used to produce pharmaceutical and industrial crops during the previous season.

Government Role

- APHIS conducts inspections at least seven times before, during, and after production.
- APHIS audits field trial records.
- APHIS partners with state departments of agriculture in the regulatory oversight of biotech crops. State officials review all proposed field tests, and APHIS-BRS requires both a permit and the concurrence of individual state departments of agriculture or other relevant agencies to import or ship any GE organisms that have the potential to be plant pests. APHIS has never approved a field test permit over the science-based objections of State counterparts or without accommodating additional permit conditions recommended by the States.

Compliance With APHIS Regulations

Developers must comply with APHIS regulations when field-testing pharmaceutical and industrial crops. A new compliance and enforcement unit was established in October 2003 to ensure adherence to permit conditions. BRS' compliance unit is dedicated solely to ensuring that companies and organizations maintain compliance through defined procedures that include violation-prevention efforts, risk-based criteria for quality inspection, uniform enforcement, and thorough documentation of any compliance infractions. Compliance specialists and inspectors from APHIS' Plant Protection and Quarantine program perform targeted inspections and audits of field tests and use set criteria to thoroughly evaluate all potential compliance infractions. Pharmaceutical and industrial field-test sites are inspected by APHIS five times during a single growing season and twice during the subsequent growing season to ensure that the conditions set forth by BRS are carefully followed.

BRS will continue to strengthen approaches to regulating the field testing of pharmaceuticals and industrials to keep pace with emerging changes in science and technology.

Additional Information

For more information about the permitting process for pharmaceutical and industrial crops, contact

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